USSN: 10/809,176

Attorney Docket: 2003.002 US

Response to Office Action of September 21, 2007

Amendments to the Specification:

Please amend the paragraph bridging line 34 on page 3 and line 10 on page 4 in the

following manner:

In the present invention a new IBDV mutant has been constructed based on a classic IBDV by

introducing mutations in the VP2 coding region such that the VP2 protein expressed by the virus

comprises virus neutralising epitope 67 that is typical for variant IBDVs. The inventors found

that in the context of a classic VP2 protein the reactivity with moab 67 is influenced by amino

acid sequences located about 100 amino acids apart. Furthermore, the assumption made by

Vakharia et al. that 286 (IIe), 318(Asp) and 323 (Glu) influence the presence of the 67 epitope is

not correct. In fact the inventors have found that the emergence of the 67 epitope in the context

of a classic IBDV VP2 protein depends on the exchange of proline at position 222 to serine or

threonine and on the presence of certain amino acid sequences in positions 318-322. The

exchange of proline to serine or threonine at position 222 in the presence of the amino acid

sequences naturally present in a classic IBDV VP2 protein at positions 318-323 (Gly-Gly-Gln-

Ala-Gly-Asp) (SEQ ID NO:1) lead to the emergence of the 67 epitope in a classic IBDV VP2

protein.

Please <u>amend</u> the paragraph bridging line 34 on page 13 and line 27 on page 14 in the

following manner:

Amino acids located in the sequence of strain D78 at position 222 (proline), 318 (glycine), 321

(alanine), and 323 (aspartate) were exchanged to amino acids serine, threonine (P222S, P222T),

aspartate, asparagine (G318D, G318N, glutamate (A321E), and glutamate (D323E), respectively,

in different combinations (see Table 4). Exchange of proline in position 222 to serine resulted in

an additional reactivity of moab 67 if the aa sequence of aa from position 318 to 323 was of

following combinations: GGQAGD (SEQ ID NO: 10), DGQAGD (SEQ ID NO: 12),

DGQAGE (SEQ ID NO: 13), GGQAGE (SEQ ID NO: 2), NGQAGE (SEQ ID NO: 5). The

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remaining combinations of the aa sequence from position 318 to 323 (DGQEGD (SEQ ID NO: 7), DGQEGE (SEQ ID NO: 34), GGQEGD (SEQ ID NO: 6), GGQEGE (SEQ ID NO: 35), NGQAGD (SEQ ID NO: 15), NGQEGD (SEQ ID NO: 8), NGQEGE (SEQ ID NO: 9)) seems to prevent the folding of the epitope characterized by moab 67 even if proline at position 222 was exchanged to serine. Binding of moab 57 was detected after exchange of aa 321 from alanine to glutamate independent if amino acid 222 (proline), 318 (glycine), and 323 (aspartate). But the exchange of arginine to serine at position 330 influenced the presence of the 57 epitope. Here if the performed exchange (R330S) was performed in presence of the combinations DGQEGD (SEQ ID NO: 7), NGQEGD (SEQ ID NO: 17), and NGQEGE (SEQ ID NO: 18), respectively, no reactivity with moab 57 was detected after co-transfection experiments. In contrast, the exchange R330S showed no influence on the reactivity with moab 57 in presence of the combination GGQEGD (SEQ ID NO: 6). The presence of reactivity of moab 57 and R63 excluded each other in the performed experiments since if the 57 epitope was present the R63 epitope was absent. Furthermore reactivity with moab R63 after co-transfection experiments was recorded after usage of plasmids encoding combinations GGQAGD (SEQ ID NO: 10), DGQAGD (SEQ ID NO: 12), DGQAGE (SEQ ID NO: 13), GGQAGE (SEQ ID NO: 2), NGQAGD (SEQ ID NO: 15), and NGQAGE (SEQ ID NO: 5) from aa 318 to 323 located in the VP2 region independent if aa 222 (proline) or aa 330 (argenine) was exchanged. Translated protein of cRNA of plasmids encoding the amino acid sequence DGQEGE (SEQ ID NO: 34) or GGQEGE (SEQ ID NO: 35) from position 318 to 323 of the polyprotein gene reacted only with the moab 69. Here also the exchange of aa 222 and/or 330 seems to have no influence on the reactivity. After all transfection experiments cells were freezed/thawed and the obtained supernatant was passaged. In each case viable virus was generated indicating that the performed mutagenised amino acids had no influence on viability and infectivity of cell culture of the virus.

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Please insert the following text after the heading on page 25, on line two:

TABLE 7

[SEQ ID NO: 37]
174 184 194 204 214 224 GB02 VLSLPTSYDLGYVRLGDPIPAIGLDPKMVATCD-
SSDRPRVYTITAADDYQFSSQYQSGG 52-70
P 002-73P UK661
Q Var-E
NT GLS
T 234 244 254 264 274 284 GB02 VTITLFSANIDAITSLSIGGELVFHTSVQGLA-
LNATIYLIGFDGTTVITRAVASDNGLTT 52-70
AA 002-73N-VQVTAGA UK661
QI-GAA Var-AVKS-V-GA
ANA Var-EVKS-V-GAANA GLS
VKHS-V-GSAAN 294 304 314 324 334 344 GB02
GIDNLMPFNLVIPTNEITQPITSIKLE- IVTSKSGGQAGDQMSWSASGSLAVTIHGGNYPG
52-70 -TSS
LN UK661 -TIS Var-A
GLS -T 354 GB02 ALRPVTLVAYER
52-70